REMARKS

This Reply is responsive to the Office Action dated October 21, 2003. Entry of the amendments and remarks submitted herein and reconsideration of the claimed subject matter pursuant to 37 CFR §1.112 is respectfully requested.

I. Amendments to the Specification and the Claims

The specification has been amended above to delete reference to SEQ ID Nos 12, 13, 14 and 15, which were inadvertently omitted from the present application. These sequences are not required to practice the claimed invention.

The specification has also been amended to include the appropriate section headings, and to include a brief description of Figure 1. Support for the description may be found at page 8, lines 6-9 of the specification.

Claim 2 has been canceled, and claim 1 has been amended to indicate that the claimed polypeptides have PMK activity and possess at least 90% identity to SEQ ID No. 7. Support for these amendments may be found in the specification, for instance at page 4, line 17, and page 2, lines 15-16. Claim 15 has been amended to maintain consistency with the elected subject matter.

No prohibited new matter has been added by way of these amendments.

II. Objections to the Specification

The specification was objected to for failing to include the appropriate application sections, and specifically for failing to include a brief description of Figure 1. The specification has been amended above to include the appropriate section headings, and to

include a brief description of Figure 1. Withdrawal of the objection is respectfully requested.

The specification was also objected to for including SEQ ID Nos. referencing sequences that were not included in the application. The specification has been amended above to delete the SEQ ID Nos. 12-15. Withdrawal of the objection is respectfully requested.

III. Rejection under 35 U.S.C. §112, First Paragraph

Claims 1, 2, 10 and 15 were rejected under 35 U.S.C. §112, first paragraph for containing subject matter that was allegedly not described in the specification in such a way so as to reasonably convey to one skilled in the art that the inventors had possession of the claimed invention at the time the application was filed. Essentially, the Examiner asserts that the application fails to provide a representative number of species to sufficiently describe a genus of polypeptides having at least 80% similarity to SEQ ID No. 7 as claimed. Applicants respectfully traverse the rejection.

At the outset, Applicants respectfully note that independent claim 1 has been amended above to cover polypeptides having phosphomevalonate kinase (PMK) activity comprising the amino acid sequence depicted in SEQ ID No. 7 or a sequence possessing at least 90% identity thereto. In addition, claim 2, directed to an isolated polypeptide of at least 15 contiguous amino acids of the polypeptide of claim 1, has been canceled. Accordingly, the invention no longer embraces any substitution, insertion or deletion resulting in at least 80% similarity to SEQ ID No. 7, but rather includes only functional variants having a sequence that is at least 90% identical to SEQ ID No. 7.

The specification discloses that nucleotide changes or mutations may be introduced into a polynucleotide sequence by *de novo* polynucleotide synthesis, by site directed mutagenesis using appropriately designed oligonucleotide primers or by any other convenient means known in the art (page 8, lines 12-15). The specification also describes numerous ways to screen for PMK activity, including the use of assays that measure increase in ADP production, assays that measure loss of ATP, and assays that monitor the transfer of a radioactive label into phosphomevalonate (page 11, line 10, to page 12, line 2). Given that the application clearly describes how to make and screen for functional variants, one of skill in the art would immediately see that the inventors were in possession of at least a genus of proteins having phosphomevalonate kinase (PMK) activity and a sequence with at least 90% identity to SEQ ID No. 7.

According to the Written Description Guidelines (FR, Vol. 66, No. 4, page 1099, January 5, 2001), "[a]ctual reduction to practice may be crucial in the relatively rare instances where the level of knowledge and level of skill are such that those of skill in the art cannot describe a composition structurally, or specify a process of making a composition by naming components and combining steps" (with emphasis, see page 1101). In fact, the Guidelines state at page 1106 that:

> An applicant may show that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics which provide evidence that applicant was in possession of the claimed invention, i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. What is conventional or well known to one of ordinary skill in the art need not be disclosed in detail. If a skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly

> described in the specification, then the adequate description requirement is met. (With emphasis.)

Applicants have identified a novel protein in *C. albicans*, PMK, and have disclosed its sequence and function. Thus, Applicants have described the relevant identifying characteristics of the novel protein. Isolation of functional variants having at least 90% identity was conventional at the time the application was filed and one of skill in the art would clearly consider the Applicants to be in possession of this genus of functional variants at the time the application was filed.

In view of the amendments and remarks above, reconsideration and withdrawal of the rejection of under §112, first paragraph for lack of written description is respectfully requested.

Claims 1, 2, 10 and 15 were rejected under 35 U.S.C. §112, first paragraph, because the specification, while being admittedly enabling for an isolated and purified polypeptide comprising the amino acid sequence, SEQ ID No. 7, a method to identify compounds that inhibit PMK activity of *C. albicans* by contacting a test compound with the polypeptide SEQ ID No. 7, and a diagnostic kit comprising antibodies that bind to SEQ ID No. 7, allegedly fails to enable sequences possessing at least 80% similarity to SEQ ID No. 7 and isolated polypeptides having at least 15 contiguous amino acids thereof, and methods and kits for detecting the same. According to the Office Action, while recombinant and mutagenesis techniques are known, it is allegedly not routine in the art to screen for multiple modifications of other types with a reasonable expectation of success in obtaining similar activity. Further, the Examiner relies on Houghten *et al.* for the premise that point mutations at one key antigen residue could eliminate antibody

recognition, and therefore, any fragment or variant will not work in a diagnostic kit or a method to identify compounds that inhibit PMK activity. Applicants respectfully traverse the rejection.

First, Applicants again respectfully note that independent claim 1 has been amended above to cover polypeptides having phosphomevalonate kinase (PMK) activity comprising the amino acid sequence depicted in SEQ ID No. 7 or a sequence possessing at least 90% identity thereto. In addition, claim 2, directed to an isolated polypeptide of at least 15 contiguous amino acids of the polypeptide of claim 1, has been canceled. Accordingly, the invention no longer embraces any substitution, insertion or deletion resulting in at least 80% similarity to SEQ ID No. 7, but rather includes only functional variants having a sequence that is at least 90% identical to SEQ ID No. 7. Variants that retain PMK function as now claimed may certainly be used in diagnostic kits to identify compounds that inhibit PMK activity.

Further, while the Examiner may be correct that mutation of a single amino acid may eliminate antigen recognition by a single antibody, it is equally true that most proteins can accommodate numerous mutations while still retaining function and antibody binding. This is evident from the fact that many proteins exist in different allelic forms in nature and there are numerous publications of functional mutant forms of proteins that include substitution mutations, truncations, and additions (including fusion proteins). The state of the art at the filing date of the invention was such that it was well within the capabilities of a person skilled in the art to perform targeted or random mutagenesis on a protein sequence and test the activity or the immunogenicity of the mutant proteins.

For instance, as noted above, the specification discloses that nucleotide changes or mutations may be introduced into a polynucleotide sequence by *de novo* polynucleotide synthesis, by site directed mutagenesis using appropriately designed oligonucleotide primers or by any other convenient means known in the art (page 8, lines 12-15). The specification also describes numerous ways to screen for PMK activity, including the use of assays that measure increase in ADP production, assays that measure loss of ATP, and assays that monitor the transfer of a radioactive label into phosphomevalonate (page 11, line 10, to page 12, line 2). Given that the application clearly describes how to make and screen for functional variants, the application certainly teaches one of skill in the art how to make functional variants in a manner reasonably correlated with the scope of the amended claims.

In view of the amendments and remarks above, reconsideration and withdrawal of the rejection of under §112, first paragraph for lack of enablement is respectfully requested.

This reply is fully responsive to the Office Action dated October 21, 2003. Therefore, a Notice of Allowance is next in order and is respectfully requested.

Except for issue fees payable under 37 CFR §1.18, the commissioner is hereby authorized by this paper to charge any additional fees during the pendency of this application including fees due under 37 CFR §1.16 and 1.17 which may be required, including any required extension of time fees, or credit any overpayment to Deposit Account 50-0310. This paragraph is intended to be a **CONSTRUCTIVE PETITION FOR EXTENSION OF TIME** in accordance with 37 CFR §1.136(a)(3).

If the Examiner has any further questions relating to this Reply or to the application in general, he or she is respectfully requested to contact the undersigned by telephone so that allowance of the present application may be expedited.

Respectfully Submitted,
Morgan Lewis & Bockius LLP

Date: February 23, 2004

By: Elizabeth C. Weiman
for Bonnie Weiss McLeod Reg. No. 44,478
Reg. No. 43,255

Customer No. **09629**
Morgan Lewis & Bockius LLP
1111 Pennsylvania Avenue, N.W.
Washington, D.C. 20004
Tel. No.: 202-739-3000
Fax No.: 202-739-3001